G 4313d

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3145

September 23, 2003

Ref: 2003-DAL-WL-22

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. William A. Simmons, President
Garland Welding Supply Co., Inc.
1960 Forest Lane
Garland, Texas 75042

Dear Mr. Simmons:

During an inspection of your compressed medical gas manufacturing/repacking facility located at 1960 Forest Lane in Garland, Texas, conducted on May 23-29, 2003, our investigators documented deviations from the Current Good Manufacturing Practice (CGMP) Regulations (Title 21, Code of Federal Regulations, Parts 210 & 211). These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). Specific deficiencies include:

- Failure to test each batch of drug product for conformance to final specifications including identity and strength prior to release [21 CFR 211.165(a)]. For example:

    - The incoming liquefied Oxygen USP in the stand tank is not being tested. After receipt of a new batch of the bulk liquid in the stand tank, vehicle mounted vessels (VMV's) are filled and tested. The analytical results obtained from the filling of the first VMV is recorded as the analytical results for the incoming bulk product in the stand tank. Analytical results so obtained are not a reliable measure of the purity and identity of the liquefied Oxygen USP batch in the stand tank. What they actually measure are the purity and identity of a blend of the product from the stand tank and the residual product in the VMV that may be different in composition.

- The Oxygen USP – Filling and Assay form, used to document the receipt, testing and release of incoming bulk Oxygen USP, contains analytical data that is pre-filled (i.e., already written) on the blank form. For example:
  - Assay results are pre-filled with the Value "99."
  - Odor tests results are pre-filled with the designation "ND." which is the designation for "none detected."
  - The blank form includes a statement: " Results DO...DO NOT conform to USP requirements." However, the word "DO" has been pre-circled on the blank forms.

- Failure to establish written sampling and testing procedures for analytical testing of finished drug product and failure to assure adequate calibration of laboratory analytical instruments used for the determination of drug product's conformance to established specifications, including identity and purity [21 CFR 211.160(b)(1) and 211.160(b)(4)]. For example:
  - There are no written procedures that describe the performance of finished product testing.
  - UHP Oxygen cylinder serial number [redacted], received in September 2002, was used as the calibration span gas for the Servomex [redacted] Oxygen Analyzer instrument, which is used for the purity and identity testing of both the incoming bulk Oxygen USP and the Oxygen USP finished product in the VMVs. However, the assay values from a previous calibration span gas, UHP Oxygen cylinder serial number [redacted] were being used instead. No certificate of analysis was on file for the calibration span gas, UHP Oxygen cylinder serial number [redacted]

- Failure to establish responsibilities applicable to the Quality Control Unit (QCU) for approving and rejecting all procedures and specifications that impact on the strength, quality, and purity of drug products and failure to ensure those QCU responsibilities and procedures are followed [21 CFR 211.22 (c) and (d)]. For example:
  - The responsibilities and procedures applicable to the QCU are not written nor is there documentation of their performance.

- Failure to adequately review and approve production records for a drug product to determine compliance with all established, approved written

procedures prior to its release and distribution [21 CFR 211.192]. For example:

- A review of the Oxygen USP Cryogenic Liquid Production and Assay Records, used to document the manufacture of liquefied Oxygen USP, is not being performed prior to the release of the product. These records are not reviewed until the end of the production day and during this time, one or more VMV's may have been filled, analyzed, and distributed.

- The filling of VMV's was documented on January 11, 2003 and March 15, 2003. However, these records were signed as reviewed and approved by the QCU on January 10, 2003 and March 14, 2003, respectively. The records were not reviewed by the QCU afterwards and the same individual who performed the subsequent fillings, also had performed the QCU review on the previous days.

- Since January 3, 2003, at least thirty-eight (38) of 100 records for Oxygen USP production document that the same individual filling VMV's also performed the analysis and the QCU review for those fillings and released the product as acceptable.

- On February 10, 2003, bulk Oxygen USP batch [redacted] was received and the QCU released this batch on February 12, 2003. However, a VMV was filled with this batch and released on February 11, 2003.

- On March 20, 2003, bulk Oxygen USP batch [redacted] was received. This batch was not accepted by the QCU. However, two (2) VMV's were filled with this batch and released on March 21, 2003.

- On April 3, 2003, bulk Oxygen USP batch [redacted] was received and the QCU released this batch on April 9, 2003. However, nine (9) VMV's were filled with this batch and released on April 7, 2003.

- Since January 3, 2003, at least ten (10) of forty (40) records for receipt of incoming bulk Oxygen USP document that the same individual who performed the analysis also performed the QCU review and released the bulk product for manufacturing.

- Failure to establish adequate written procedures for production and process control in that the procedures used have not been reviewed and approved by a quality control unit [21CFR 211.100(a)]. For example:

- The current written policies and procedures were adopted from SOPs of your supplier and these SOPs were implemented without approval by the QCU.

- Failure to conduct GMP training with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to their responsibilities [21 CFR 211.25(a)]. Documentation collected during the inspection shows that employees have insufficient knowledge of CGMP requirements. In addition, there is no record of GMP training to correct these deviations. For example:

  - Since January 3, 2003, at least thirty-eight (38) of 100 records documenting the production of liquid Oxygen USP showed that the filling, analysis, and review was performed by the same individual.

  - Since January 3, 2003, at least seven (7) records that pertain to the production of liquefied Oxygen USP failed to include a review by a second individual.

  - Since January 3, 2003, at least nine (9) of forty (40) records that pertain to the receipt of liquefied Oxygen USP in bulk, contained incorrect lot numbers, incorrect dates of analysis, missing signatures, incorrect supplier batch numbers, or missing analytical results.

  - Records dated January 11, 2003 and March 15, 2003, document the filling of VMV's for which a production record had been reviewed and approved by the QCU on the previous days of January 10, 2003 and March 14, 2003, respectively. The records were not reviewed again by the QCU. The same individual who performed the fillings had also performed the QCU reviews on the previous days.

  - Spot checks are performed to determine the need for training. However, the interval for conducting these spot checks is not specified, nor is there documentation of remedial training that was given as a result of these checks.

- Failure to establish written procedures in sufficient detail that describe the receipt, storage, sampling, testing, approval, and rejection of components [21 CFR 211.80(a)]. For example:

  - There are no written procedures describing the receipt of bulk liquefied Oxygen USP from the supplier or procedures describing the release for use in manufacturing.

- Failure to perform periodic calibrations of laboratory analytical instruments used for the determination of drug product's conformance to established specifications including strength and purity [21 CFR 211.194(d)]. For example:

    - There is no documentation of the calibration of the Servomex [redacted] Oxygen Analyzer instrument, which is used to perform purity and identity testing on both the incoming liquefied Oxygen USP and the Oxygen USP finished product.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all drug warning letters, so that they may take this information into account when considering the awarding of contracts.

We are aware of your firm's commitment to correct various deficiencies documented during the inspection and we received your firm's written response dated June 2, 2003. While the submitted revisions for your QCU describe the authorities and responsibilities applicable to the QCU, these revisions do not include procedures describing how the QCU is to accomplish their assigned responsibilities or to whom specific activities are assigned. We acknowledge your firm's commitment to provide increased personnel training in the subject of drug CGMP's. However, the letter failed to specify the dates for this training, the subjects to be presented, the targeted audience, the length of the training, or the frequency of the periodic training involving drug CGMP's. Your letter indicated that all filling records using the incorrect calibration gas, UHP Oxygen cylinder serial number [redacted] have been changed to reflect the correct calibration gas, UHP Oxygen cylinder serial number [redacted]. However, there was no indication that a review of all batch records since September 2002 was done to adjust the calculations, as necessary, using the certificate of analysis (COA) values provided with the correct calibration gas. Your response also does not indicate whether the assay values on the COA's for these 2 calibration gases were compared to determine if there was a need to adjust the calculations attained by using the COA provided with the incorrect calibration gas.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction.

Please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be sent to the Food and Drug Administration,

Dallas District Office, Attention: Brenda C. Baumert, Compliance Officer, at the above letterhead address.

Sincerely,

Sylvia Y. Lyett

SOL

Michael A. Chappell
Dallas District Director

MAC: bcb